



Atty Dkt. No.: UCSF-048 CIP  
USSN: 09/254,988

CERTIFICATE OF MAILING			
I hereby certify that the correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.			
Typed or Printed Name	Matthew Ottis		
Signature		Date	01-17-01
<b>DECLARATION OF LESLIE BENET UNDER 37 C.F.R. § 1.132</b>  Address to: Assistant Commissioner for Patents Washington, D.C. 20231		Attorney Docket	UCSF-048 CIP
		First Named Inventor	M. German
		Application Number	09/254,988
		Filing Date	June 11, 1999
		Group Art Unit	1633
		Examiner Name	D. Nguyen
		Title	<i>Delivery of therapeutic gene products by intestinal cell expression</i>

Dear Sir:

1. I, Leslie Benet, declare and say I am a resident of San Francisco, California. My residence address is 601 Van Ness Ave. Apt. 451, San Francisco, CA 94102.

2. I hold a Bachelor degree in Pharmacy, which I received from University of Michigan in 1960. I further hold a Ph.D. degree which I received from University of California, San Francisco, in 1965. I am an expert in the fields of pharmacokinetics, biopharmaceutics, and drug delivery, and as such am familiar with the accepted practice in drug delivery as of September 19, 1996, i.e., the priority date of the above-captioned patent application. A copy of my curriculum vitae is provided herewith as Exhibit 2.

3. I understand that the Examiner in the above-captioned patent application would like to see evidence that those in the field of drug delivery accept gavage as a model in experimental animals for oral delivery.

4. Preclinical testing of oral drugs usually involves data collected in rodents. Commonly, oral drugs are administered to rats and mice by gavage, a method of feeding that allows for exact dose control. Oral gavage employs a stomach tube or "cannula" that is briefly

inserted through the mouth, down the esophagus, and into the lumen of the stomach. Test compounds are then instilled directly from the mouth into the stomach via the catheter, and the catheter is removed. Materials delivered by gavage, like all oral drugs, then follow the natural course of digestion and pass out of the stomach through the pyloric canal into the upper small intestine or duodenum.

5. Gavage is an accepted way in the field of drug delivery to introduce a drug orally into experimental animals. Gavage has been used for several decades as a means of oral administration of various substances to experimental animals in lieu of oral administration because animals do not readily orally ingest drugs. It is preferable because the technique provides for more precise control of oral dose administered.

6. The publications provided with this Declaration are reports from various investigators who, to test oral compounds, have used gavage in experimental animals as the conventional model for oral administration. These publications attest to the fact that gavage is an accepted way in the field to accurately simulate oral delivery of test compounds into experimental animals.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such will false statements may jeopardize the validity of the application or any patent issuing thereon.

1/16/01  
Date

Leslie Benet  
Dr. Leslie Benet

Attachments: Exhibit 2: Curriculum vitae of Dr. Leslie Benet  
Exhibits 3-19: References